

PROPATH

THE FOCUS

Immunohistochemistry

Endocervical vs. Endometrial Adenocarcinoma

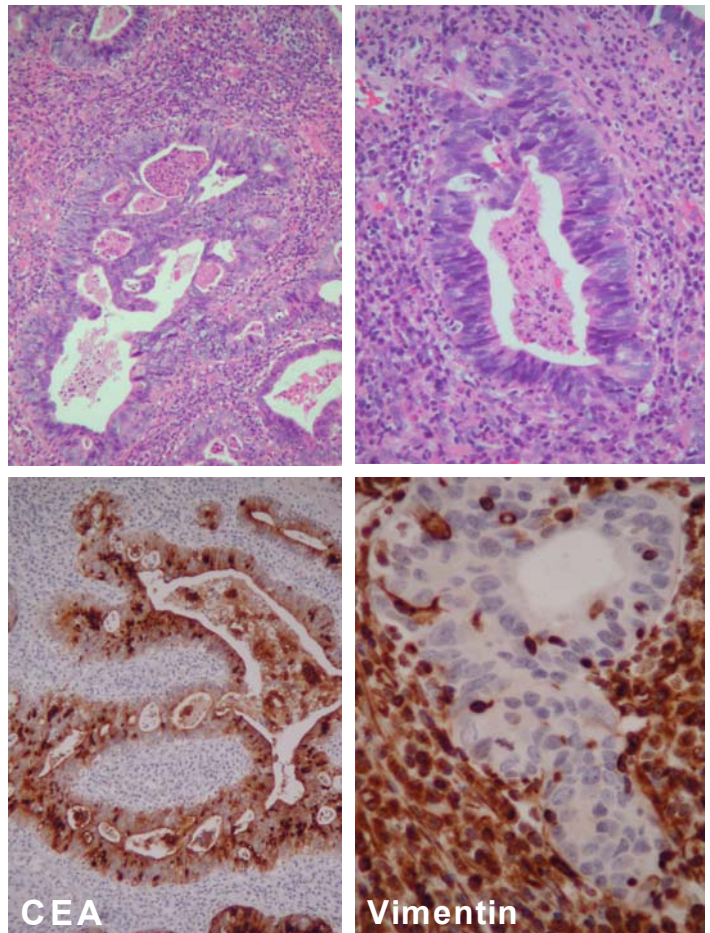
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The morphologic overlap of endometrial and endocervical adenocarcinoma can make distinction difficult on H&E. This distinction is important, since the choice of initial therapy may differ substantially, and there are also differences in chemotherapeutic agents used to treat advanced cases of these tumors. The January 2002 issue of the *International Journal of Gynecological Pathology* contains 2 papers addressing this problem, as well as an excellent editorial (authored by Dr. Richard Zaino) that nicely summarizes the current state of affairs with respect to this problem.

The first paper (authored by Castrillon and associates from Brigham and Women's Hospital) described a study of 30 endometrial adenocarcinomas and 29 endocervical adenocarcinomas. It included cases that showed overlapping morphologic features, as 15/29 of the endocervical adenocarcinomas showed endometrioid differentiation, and 16/30 of the endometrial adenocarcinomas showed mucinous differentiation. Both sets of tumors were cytokeratin 7 positive and cytokeratin 20 negative. CEA was more common in endocervical adenocarcinomas (62%), than in endometrial adenocarcinomas (27%). The authors also noted that CEA appeared to be particularly useful for tumors that had endometrioid morphology, since only 14% of the endometrial endometrioid adenocarcinomas were CEA positive, in contrast to 67% of the endocervical adenocarcinomas with endometrioid morphology. 97% of the endometrial adenocarcinomas were vimentin positive, often showing a characteristic lateral cell border or perinuclear pattern of reactivity. In contrast, only 7% of the endocervical adenocarcinomas were vimentin positive. The second study (authored by McCluggage and associates from Belfast, Northern Ireland) evaluated 30 endometrioid endometrial adenocarcinomas and 26 endocervical adenocarcinomas of endocervical type. In their study, 93% of endometrial adenocarcinomas were strongly estrogen receptor (ER) positive, whereas focal weak ER positivity was noted in 38% of

endocervical adenocarcinomas. Vimentin was diffusely positive in 97% of the endometrial adenocarcinomas, but in only 8% of the endocervical adenocarcinomas. Prior studies have reported ER in 70% of endometrial adenocarcinomas, in contrast to 10-20% of endocervical adeno-



36 year-old female with an abnormal pap smear underwent cervical biopsy, and was found to have an invasive adenocarcinoma in the endocervix. H&E examination (top two frames) could not exclude endocervical involvement by an endometrial carcinoma. The tumor cells were strongly and diffusely positive for CEA (bottom left) and negative for vimentin (bottom right), allowing a diagnosis of primary endocervical adenocarcinoma to be made.

carcinomas, vimentin reactivity in 50-81% of endometrial adenocarcinomas vs. <13% of endocervical adenocarcinomas, and CEA in 65-95% of endocervical adenocarcinomas. In light of these results, a relatively small panel of immunostains including **vimentin**, **monoclonal CEA**, and **ER** is reasonable to address the problem of distinguishing endometrial from endocervical adenocarcinoma. In difficult cases, some authors have also employed in situ hybridization for HPV DNA, which if positive can be useful in supporting the interpretation of endocervical origin. Expected immunoreactivity is summarized in the table below:

	<u>Vimentin</u>	<u>CEA</u>	<u>ER</u>
Endom	+(>70-93%)	usually -	70-90% strong +
Endocx	-(7-8%+)	65-95%+	-(10-20%+, 38% weak)

Therefore, the "classic" endometrial adenocarcinoma will be positive for vimentin and ER, but negative for CEA. In contrast, the "classic" endocervical adenocarcinoma will be CEA positive and negative for both vimentin and ER.

Another antibody that may be of use in this differential diagnosis is MUC5AC, although currently there is insufficient published data to know for certain. MUC5AC is negative in normal endometrial glands and is positive in normal endocervical glands. I have

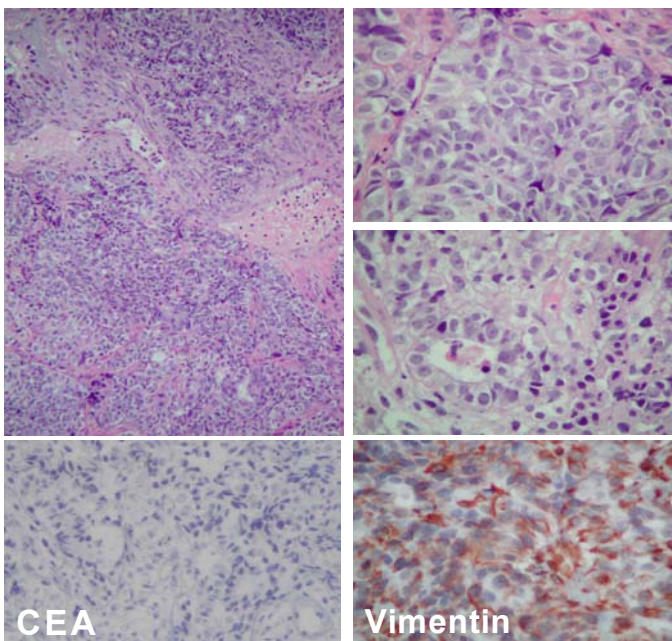
observed strong reactivity of this marker in several cases of endocervical adenocarcinoma, but it has also been focally positive in several endometrioid adenocarcinomas. Similarly, N-cadherin may have potential use in this differential diagnosis, as N-cadherin is positive in normal endometrial glands and in most cases of endometrioid adenocarcinoma, but is negative in most normal endocervical glands. I have not personally studied enough cases of endocervical adenocarcinoma to know whether most endocervical adenocarcinomas are N-cadherin negative, although I think it would be worth studying that question.

REFERENCES:

1. Zaino RJ: The Fruits of Our Labors: Distinguishing Endometrial from Endocervical Adenocarcinoma (Editorial). *International Journal of Gynecological Pathology* 21 (1): 1-3, 2002.
2. Castrillon DH, Lee KR, Nucci MR: Distinction between Endometrial and Endocervical Adenocarcinoma: An Immunohistochemical Study. *International Journal of Gynecological Pathology* 21 (1): 4-10, 2002.
3. McCluggage WG, Sumanthi VP, McBride HA et al: A Panel of Immunohistochemical Stains, Including Carcinoembryonic Antigen, Vimentin, and Estrogen Receptor, Aids the Distinction between Primary Endometrial and Endocervical Adenocarcinomas. *International Journal of Gynecological Pathology* 21 (1): 11-15, 2002.

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47 year-old female with uterine bleeding had D&C, and a poorly differentiated adenocarcinoma was found (H&E stains, top three frames). The tumor was negative for CEA (bottom left) and positive for Vimentin (bottom right), demonstrating the "classic" phenotype of endometrial adenocarcinoma.

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